Do Elderly Patients With Non-hematologic Malignancies Have a Worse Outcome in the ICU?

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SUMMARY

Background: The aim of this study was to evaluate the difference in outcome between older (≥65 years) and younger (<65 years) cancer patients admitted to the intensive care unit (ICU) with acute life-threatening illness.
Methods: A total of 1,881 patients were admitted to the medical intensive care unit (ICU) of Mackay Memorial Hospital, Taipei, from September 2004 to September 2007. We excluded patients diagnosed with cancer and in remission for >5 years, ICU stay of <24 hours, and ICU admission for routine postoperative monitoring. A total of 85 patients were included and divided into younger (<65 years) and older (≥65 years) groups for comparison.
Results: The mean ages of the younger and older group were 50.7±3.6 years and 76.1±1.9 years, respectively. There was no significance in ICU length of stay (8.6±2.5 days vs. 11.7±2.6 days; $p=0.09$), in the proportion of high Adult Comorbidity Evaluation 27 grade (86.1% vs. 77.6%; $p=0.32$). The most frequent reasons for ICU admission in the younger and older groups were acute respiratory failure (50.0% vs. 61.2%) and shock (41.7% vs. 24.5%). The elderly had significantly more sepsis (87.8% vs. 58.3%; $p=0.002$) and bloodstream or intraperitoneal infection (34.7% vs. 13.9%; $p=0.03$), and received earlier conventional mechanical ventilation (–0.3±0.17 days vs. 0.13±0.36 days; $p=0.045$) and shorter vasopressor administration (2.07±0.94 days vs. 5.36±2.63 days; $p=0.03$). The hospital survival times in younger and older groups were 36.3±16.3 days and 60.9±33.9 days ($p=0.20$), respectively, and 1-year survival rates were 2.8% and 12.2% ($p=0.12$), respectively.
Conclusion: The main cause of death and survival rates, both short-term and long-term, were not worse in elderly patients with non-hematologic malignancies in the ICU, and the main reasons for patient death were sepsis and respiratory failure, rather than the malignancy itself. Therefore, an ICU admission policy should not exclude elderly patients with non-hematologic malignancies merely because of concerns about survival rate or life expectancy. [International Journal of Gerontology 2009; 3(4): 209–216]

Key Words: elderly, intensive care units, neoplasms, treatment outcome

Introduction

The aged population in Taiwan (≥65 years of age) had increased to 10.33% of the total population in 2008 and is predicted to be over 20% in 2026[1,2]. In 2007, malignant neoplasms were the most common cause of death, of which lung cancer, liver and intrahepatic bile duct cancer, and colorectal cancer were the leading malignancies[3].

Previous studies[4–6] had recognized the low survival rate in cancer patients requiring life-sustaining treatment. Because of the difficulty in assessing quality of care, the intensive care unit (ICU) costs[5], the restriction of medical resources, and the concepts of end-of-life (EOL) care, the intensivist found it frustrating to provide clinical decision making for patients admitted to the ICU, especially for those elderly patients with underlying malignancies.

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In the past two decades, advances in cancer treatment and supportive care have improved the survival rate of cancer patients, but have been associated with more complications of these treatments and has thus led to the need for intensive care for accompanying acute illness[7]. Therefore, intensive care for patients with cancer does not merely function as advanced supportive care for the end of life, but also as care for complications of cancer treatment. A previous study did not find the cause of admission or the nature of malignancy predicted outcome satisfactorily[8]. Older age has been found to be one of the negative survival predictors. However, comparisons of the outcomes between older and younger patients with cancer requiring intensive care have not been reported. Thus, the aim of this study was to evaluate the differences in outcome between older (≥65 years) and younger (<65 years) cancer patients admitted to the ICU with acute life-threatening illness.

Materials and Methods

This retrospective study reviewed the medical records of patients admitted to the medical ICU in Mackay Memorial Hospital, Taipei, between September 2004 and September 2007. Mackay Memorial Hospital is a tertiary teaching hospital. The medical ICU contains 27 beds for the care of critically ill adult patients. The decisions to admit patients with cancer to medical ICU are made by the primary physician and intensivist. Generally, no patient is denied access to ICU care under the policy of the hospital administration. All patients with underlying non-hematologic malignancies, who were admitted to medical ICU, were included in this study. The exclusion criteria for further analysis were as follows: (1) diagnosis of cancer with >5 years' remission, (2) ICU stay of <24 hours, and (3) ICU admission for routine postoperative care. In patients with multiple ICU admissions, we recorded only the first admission.

The Logistic Organ Dysfunction (LOD) score[9] and the Adult Comorbidity Evaluation 27 (ACE-27) grade[10] were calculated at ICU admission. Acute renal failure was defined as serum creatinine elevation (>1.5× baseline value), decreased calculated creatinine clearance (<0.75× baseline creatinine clearance estimated using the Cockcroft formula), or oliguria (<0.5 mL/kg/hr for 6 hours).

Sepsis was diagnosed according to the criteria of the American College of Chest Physicians/Society of Critical Care Medicine consensus conferences[11], and at least one positive microbiologic result in collected sterile specimens was acquired for confirmation of the infection source.

EOL decisions to withhold life-sustaining treatments were made if recovery from acute illness or control of underlying malignancies was not feasible and terminally progressive disease was imminent.

The following data were collected: causes of ICU admission, severity of underlying disease, ACE-27 grade, Acute Physiology and Chronic Health Evaluation (APACHE) II score, LOD scores and their difference, start and duration of all ICU treatments, length of ICU stay, and ICU and hospital mortality. The time correlation between EOL orders and deaths of patients with various types of non-hematologic malignancies during the ICU stay was also determined.

Data were analyzed using the commercially available software SPSS version 12.0 (SPSS Inc., Chicago, IL, USA) for Windows. Continuous variables were expressed as mean±standard deviation and compared using Student's t test. Categorical variables were compared using the χ^2 or Fisher's exact tests. All p values and confidence intervals were two-sided. A p value<0.05 was considered statistically significant.

Results

A total of 1,881 patients were admitted to medical ICU during the study period, 127 with non-hematologic malignancies. The following were excluded from the study: (1) 13 who had been diagnosed with cancer and had >5 years' remission; (2) 14 who had ICU stay of <24 hours; (3) seven for routine postoperative monitoring; and (4) seven with lack of data or lost to follow-up. Finally, 85 patients were included in the analysis, and they were divided into a younger group (<65 years) and older (≥65 years) group for comparison.

Patient characteristics and comparisons between the two age groups are shown in Table 1. The mean ages of the younger and older groups were 50.7±3.6 years and 76.1±1.9 years, respectively, and the majority of each group was male (69.4% vs. 53.1%). The types of cancer varied in the two groups, with the most common types of malignancies in the younger group occurring in the hepatobiliary systems (27.8%), head

Table 1. *Characteristics of malignancy in intensive care unit (ICU) patients**

	Young group (< 65 yr; $n=36$)	Elderly group (≥ 65 yr; $n=49$)	p
Age (yr)	50.7 ± 3.6	76.1 ± 1.9	
Male gender	25 (69.4)	26 (53.1)	0.13
ICU length of stay (d)	8.6 ± 2.5	11.7 ± 2.6	0.09
Multiple cancer (≥ two primary cancer)	1 (2.8)	6 (12.2)	0.12
Advanced stage of cancer	23 (63.9)	30 (61.2)	0.80
Malignancy characteristics			
Head and neck	9 (25.0)	4 (8.2)	0.03
Lung	5 (13.9)	17 (34.7)	0.03
Esophagus and stomach	2 (5.6)	7 (14.3)	0.20
Liver and bile duct systems	10 (27.8)	13 (26.5)	0.90
Colon and rectum	3 (8.3)	8 (16.3)	0.28
Others	8 (22.2)	7 (14.3)	0.34
Never received cancer treatment	11 (30.6)	22 (44.9)	0.18
Time from diagnosis (mo)	14.6 ± 5.2	9.7 ± 3.3	0.12
New diagnosis at admission	3 (8.3)	9 (18.4)	0.19
Direct admission from emergency room	14 (38.9)	12 (24.5)	0.16
APACHE II score	18.2 ± 2.6	23.5 ± 1.9	0.002
ACE-27 grade 3	31 (86.1)	38 (77.6)	0.32
Metastatic malignancy	16/31 (51.2)	22/38 (57.9)	0.60
Newly diagnosed	3/31 (9.7)	8/38 (21.1)	0.20

**Data are presented as mean ± standard deviation or n (%). APACHE II = Acute Physiology and Chronic Health Evaluation II; ACE-27 = Adult Comorbidity Evaluation 27.*

and neck (25.0%), and lung (13.9%); whereas in the elderly group, lung (34.7%), hepatobiliary systems (26.5%), and colon and rectum (16.3%) cancer were the leading types. The younger group had significantly more head and neck cancer (25% vs. 8.2%; $p=0.03$); and the elderly group had more lung cancer (34.7% vs. 13.9%; $p=0.03$).

There were no significant differences between the elderly group and the younger group in terms of ICU length of stay (11.7 ± 2.6 days vs. 8.6 ± 2.5 days; $p=0.09$), incidence of multiple cancer (12.2% vs. 2.8%; $p=0.12$), time from diagnosis of cancer to ICU admission (9.7 ± 3.3 months vs. 14.6 ± 5.2 months; $p=0.12$), newly diagnosed malignancy at ICU admission (18.4% vs. 8.3%; $p=0.19$), or ICU admission directly from the emergency room (24.5% vs. 38.9%; $p=0.16$).

There was no difference in the proportion of high ACE-27 grade cancer, which was mostly graded by metastatic cancers, and only a small portion were represented by newly diagnosed cancer, which was higher in the elderly group (21.1% vs. 9.7%; $p=0.20$). The average APACHE II score was significantly higher in the elderly group (23.5 ± 1.9 vs. 18.2 ± 2.6; $p=0.002$).

The most frequent reasons for ICU admission in the older and younger groups were acute respiratory failure (61.2% vs. 50.0%) and shock (24.5% vs. 41.7%), as shown in Table 2. Clinically significant events or complications occurring in the ICU are shown in Table 2. The elderly had significantly more sepsis (87.8% vs. 58.3%; $p=0.002$) and bloodstream or intraperitoneal infection (34.7% vs. 13.9%; $p=0.03$) than younger patients, but there was no significant difference in urinary tract infections (32.7% vs. 16.7%; $p=0.10$).

Table 3 shows the treatments in the ICU. The elderly had significantly earlier conventional mechanical ventilation (–0.3 ± 0.17 days vs. 0.13 ± 0.36 days; $p=0.045$) and shorter duration of vasopressor administration (2.07 ± 0.94 days vs. 5.36 ± 2.63 days; $p=0.03$).

Table 4 shows that there were significantly less deaths in the elderly group from massive gastrointestinal or tumor bleeding (4.1% vs. 16.7%; $p=0.049$), and no

Table 2. *Reasons for intensive care unit (ICU) admission and comorbidities in ICU patients**

	Young group (< 65 yr; *n* = 36)	Elderly group (≥ 65 yr; *n* = 49)	*p*
Reasons for ICU admission			
Shock	15 (41.7)	12 (24.5)	0.09
Respiratory failure	18 (50.0)	30 (61.2)	0.30
Unconsciousness	4 (11.1)	4 (8.2)	0.65
Cardiovascular events	3 (8.3)	0 (0)	0.04
Massive GI or tumor bleeding†	6 (16.7)	4 (8.2)	0.23
Post CPR status	2 (5.6)	5 (10.2)	0.44
Comorbidities			
Cardiovascular	4 (11.1)	8 (16.3)	0.50
Acute renal failure	15 (41.7)	25 (51)	0.39
GI or tumor bleeding‡	18 (50.0)	18 (36.7)	0.22
Sepsis			
Pneumonia	12 (33.3)	24 (49)	0.15
UTI	6 (16.7)	16 (32.7)	0.10
Others	5 (13.9)	17 (34.7)	0.03
Total	21 (58.3)	43 (87.8)	0.002
Pneumonia in ARF admission§	8/18 (44.4)	21/30 (70.0)	0.08

**Data are presented as n (%); †blood loss-related systolic blood pressure of < 90 mmHg; ‡in patients with reported active peptic ulcer or tumor bleeding; §percentage calculated as the proportion of patients with pneumonia whose ICU admission was mainly for respiratory failure. GI = gastrointestinal; CPR = cardiopulmonary resuscitation; UTI = urinary tract infections; ARF = acute respiratory failure.*

Table 3. *Treatment in the intensive care unit**

Treatment	Young group (< 65 yr; *n* = 36)	Elderly group (≥ 65 yr; *n* = 49)	*p*
Endotracheal intubation	22 (61.1)	36 (73.5)	0.23
Conventional mechanical ventilation	24 (66.7)	37 (75.5)	0.37
Start time† (d)	0.13 ± 0.36	−0.30 ± 0.17	0.045
Duration‡ (d)	9.75 ± 4.10	14.99 ± 4.78	0.11
NPPV	3 (8.3)	1 (2.0)	0.18
Start time† (d)	−2.33 ± 5.58	6	NS
Duration‡ (d)	4.90 ± 3.00	0.5	NS
Vasopressors	18 (50)	30 (61.2)	0.30
Start time† (d)	0.78 ± 1.53	3.13 ± 2.21	0.09
Duration‡ (d)	5.36 ± 2.63	2.07 ± 0.94	0.03
Emergency renal replacement therapy	3 (8.3)	4 (8.2)	0.98
Start time† (d)	5.00 ± 10.79	3.75 ± 5.08	0.85
Duration‡ (d)	5.17 ± 8.66	1.5 ± 1.65	0.50

**Data are presented as n (%) or mean ± standard deviation; †with reference to the day of intensive care unit admission; ‡calculated as 0.5 day for duration of < 24 hours. NPPV = noninvasive positive pressure ventilation; NS = not significant.*

statistical differences between the two groups in the LOD score, the proportion of do-not-resuscitate (DNR) assignment, the frequency of EOL orders, and the 30-day mortality rate after ICU discharge. The hospital survival times for younger and older groups were 36.3 ± 16.3 days and 60.9 ± 33.9 days ($p = 0.20$), respectively, and 1-year survival rates were 2.8% and 12.2% ($p = 0.12$), respectively.

Table 4. *Cause of death and analysis of do-not-resuscitate (DNR) agreement**

	Young group (< 65 yr; $n=36$)	Elderly group (≥ 65 yr; $n=49$)	p
Cause of death			
Sepsis with shock	14 (38.9)	21 (42.9)	0.71
Cardiovascular	0 (0)	1 (2.0)	0.39
Massive GI or tumor bleeding	6 (16.7)	2 (4.1)	0.049
Respiratory failure	10 (27.8)	18 (36.7)	0.38
LOD score on ICU day 1	5.61 ± 1.04	6.27 ± 0.94	0.36
LOD score on ICU day 6	5.10 ± 1.67	5.80 ± 1.24	0.51
Δ LOD score†	–0.45 ± 1.29	–0.39 ± 1.07	0.95
Received CPR	2 (5.6)	5 (10.2)	0.44
Signed DNR order	31 (86.1)	37 (75.5)	0.23
Timing of DNR agreement			
Signed after ICU admission (d)	23.0 ± 13.5	19.2 ± 11.4	0.67
Signed before death‡ (d)	1.05 ± 0.54	1.00 ± 0.38	0.86
Requested AAD on hospital discharge	10 (27.8)	18 (36.7)	0.38
ICU mortality§	15 (41.7)	23 (46.9)	0.63
Survival duration from ICU admission to death (d)	36.3 ± 16.3	60.9 ± 33.9	0.20
One-month survival after ICU discharge			
In all patients	10 (27.8)	18 (36.7)	0.38
In those who never received cancer treatment	1/11 (9.1)	5/22 (22.7)	0.34
One-year survival after ICU discharge			
In all patients	1 (2.8)	6 (12.2)	0.12
In those who never received cancer treatment	0/11 (0)	1/22 (4.5)	0.47

**Data are presented as n (%) or mean ± standard deviation; †the score on ICU day 6 minus the score on day 1; ‡calculated only for patients who signed DNR ≤ 3 days before death; §includes the patient who requested for against-advice discharge in critical condition and died within 24 hours. GI = gastrointestinal; LOD = Logistic Organ Dysfunction; CPR = cardiopulmonary resuscitation; ICU = intensive care unit; AAD = against-advice discharge.*

Discussion

It has been argued that greater allocation of intensive care resources should be available to a younger patient population, while invasive diagnostic and therapeutic procedures should be withheld from older patients, especially those critically ill patients with cancer. Such preferential medical servicing arises from the perception of the likelihood of care being futile in critically ill older cancer patients. Our study demonstrates that critically ill older patients with underlying malignancies have a similar outcome in terms of ICU and hospital mortality and mortality 1 year after hospital discharge, compared with younger counterparts. The difference in the type of malignancies is not significant, although elderly patients have slightly more lung cancer and less head–neck cancer. There is also no significant difference in the proportion of advanced cancer in the elderly patients compared with younger patients (61.2% vs. 63.9%; $p=0.80$). We found a higher, though not statistically significant, 1-year survival rate after ICU discharge in the elderly group, with most (50%) being patients with rectal cancer. It is known that different types of malignancies have different prognoses and survival rates; we need further analyses to confirm the impact on overall survival after ICU discharge.

The main indications for ICU admission were not significantly different between the two groups, with acute respiratory failure being the most common reason. A prospective 5-year observational study of 203 cancer patients showed that acute respiratory failure was mainly caused by infectious pneumonia (58%), and resulted in 44.8% ICU mortality and 47.8% hospital mortality[12]. In our study, the proportion of patients

with pneumonia who were admitted to the ICU mainly for respiratory failure was higher in the elderly group but the difference was not significant (70.0% vs. 44.4%; $p=0.08$). The elderly group had no cardiovascular events as the reason for ICU admission (0% vs. 8.3%; $p=0.04$). The significance of this factor is unknown, given such a small number of patients.

Our study reinforced the findings of previous studies[13,14], which demonstrated that age was not a negative predictor of ICU outcome, and both ICU and overall hospital mortality were lower in the elderly cancer patients. We also found that complications during the ICU stay were similar in both groups except for more infectious events in the elderly, such as sepsis (87.8% vs. 58.3%; $p=0.002$), and bloodstream or intraperitoneal infection (34.7% vs. 13.9%; $p=0.03$). Although sepsis, septic shock and respiratory insufficiency, and need for mechanical ventilation have been shown to be associated with poor outcome[15–17], such a correlation has not been demonstrated in our study, most likely because of the small patient numbers in this study.

Christodoulou et al.[17] discovered that the Eastern Co-operative Oncology Group performance scale before hospitalization was a good predictor for short-term outcome of solid tumor patients in the ICU; they also found that the APACHE II score ($p=0.001$) and multiple organ failure ($p=0.001$) were negative predictors. However, the role of the Eastern Co-operative Oncology Group scale as a predictor of tumor survival remains controversial, because there was a contrasting finding in an earlier study in 1998 by Jones et al.[18]; thus, we did not include Eastern Co-operative Oncology Group in our study design.

In our study, the older and younger patients received similar rates of endotracheal intubation, conventional mechanical ventilation, vasopressor administration, and renal replacement treatment. Lecuyer et al.[19] suggested that therapeutic decisions be postponed over the first 5 ICU days, reflecting the window for organ failure recovery. They suggested that the LOD score on ICU day 6 and the difference in LOD score between day 1 and day 6 predicted the hospital mortality more accurately. In our study, both the LOD score of the older and younger groups on ICU day 1 (6.27 ± 0.94 vs. 5.61 ± 1.04; $p=0.36$) and day 6 (5.80 ± 1.24 vs. 5.10 ± 1.67; $p=0.51$), and Δ LOD (-0.39 ± 1.07 vs. -0.45 ± 1.29; $p=0.95$) were not statistically significantly different. The LOD score had a downward trend during the ICU stay in both groups.

We tried to evaluate if the ACE-27 grading system could faithfully reflect the severity of the underlying disease. The result was disappointing, because most patients with ACE-27 grade 3 (55.1%, $n=38$ in total in the two groups) had metastatic or uncontrolled cancer. This revealed that the actual severity of chronic illness could be overestimated if patients with malignancy were enrolled in the study.

Azoulay and Afessa[20] provided a good guide for the ICU admission policy for cancer patients. In their statement, patients with newly diagnosed malignancy should receive full code management, including supportive treatment and chemotherapy. On the other hand, patients with poor functional status, underlying comorbidities and lack of available treatment might be denied admission to the ICU. Azoulay et al.[21] concluded in another study that malignancy may not be a good reason for reluctance to admit cancer patients to an ICU, especially when their ICU mortality was comparable to severely ill non-cancer patients. However, Staudinger et al.[16] warned that admission to the ICU may worsen the prognosis of a cancer patient substantially.

Lecuyer et al.[19] defined the policy more precisely. They denied ICU admission for bedridden patients, those who refused treatment or those for whom no cancer treatment options except palliative care were available. Full code management was preserved for previously untreated malignancies, acute tumor lysis syndrome, bulky or infiltrating tumors at the earliest phase of treatment, and patients in complete cancer remission.

It was interesting to note the attitude to palliative care in both groups, which may be reflected as the proportion and timing of EOL care decision making. Contrary to general belief, the frequency and timing of EOL care in the elderly group were similar to those in the younger group. An impressive survey by Sulmasy et al.[22] reported that attending physicians were more confident than nurses in discussing DNR and consent for medical procedures with the family. Although the staff nurses were more courageous than physicians in initiating DNR discussion, but they were also queried more about their role in doing so. In our study, all the DNR discussions were initiated by the physicians, whose positive attitude and detailed explanation gained more confidence from the family, and made no differences in EOL decision making in either group.

Limitations of this study

First, the small sample size in our study makes the statistical power rather low. A larger cohort study with multiple center participation is necessary for further study. Second, we excluded the postoperative patients. This exclusion may have introduced a selection bias. However, a homogeneous group of patients were included to make the comparison more clinically relevant. Third, a questionnaire may be necessary for further investigation of moral concepts. We retrospectively analyzed DNR agreements and the timing of the orders, but we could not actually determine the willingness of the family and their expectancy of EOL care. The questionnaire should at least include: (1) the degree of the patient's comfort in each management; (2) the life span of the patient expected by the nursing staff, intensivist and the family; (3) the treatment response in terminal care; (4) the degree of psychologic distress of the family after against-advice discharge in a critical condition; and (5) the satisfaction of the family after each consultation with a physician.

Lastly, we found in this study that the ACE-27 score may be increased by a newly diagnosed malignancy or metastatic tumors, which may mask the actual severity of the underlying comorbidities, resulting in a misleading outcome of the survival survey. Although we calculated the APACHE II score for adjustment, we found that it lacked comparability in such a study of different ages. Another scoring system, such as the Sepsis-related Organ Failure Assessment score, may be necessary for better adjustment for the severity of the underlying disease.

In conclusion, the elderly patients with non-hematologic malignancies had significantly more sepsis comorbidity but less gastrointestinal or tumor bleeding than the younger group, and patients in both groups mainly died of sepsis and respiratory failure, rather than the malignancy itself. Neither the short- nor long-term survival rate was impaired in the elderly cancer patients, and they even presented with better prognosis than the younger group. Therefore, an ICU admission policy should not exclude elderly patients with non-hematologic malignancies merely for concern of the survival rate or life expectancy. We have to estimate the severity of comorbidities in the patient and communicate well with the patient and his/her family about their willingness to accept the therapeutic strategy at the end of life, no matter how old he/she is. In this way, we can provide a better quality of intensive care, more precisely control medical costs, and conserve resources for those in need.

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